AMENDMENT AND RESPONSE UNDER 37 C.F.R. § 1.116 - EXPEDITED PROCEDURE

Serial Number:09/645.706 Filing Date: August 24, 2000

1.

Title: SYNTHETIC NUCLEIC ACID MOLECULE COMPOSITIONS AND METHODS OF PREPARATION

## IN THE CLAIMS

Dkt: 341.005US1

Please amend the claims as follows:

(Currently Amended) A [[first]] synthetic nucleic acid molecule comprising at least 300 nucleotides of a coding region for a reporter polypeptide which has at least 90% amino acid sequence identity to a reporter polypeptide encoded by a wild type nucleic acid sequence, wherein the codon composition of the [[first]] synthetic nucleic acid molecule is different at more than 25% of the codons from that of the wild type nucleic acid sequence and is different than the codon composition of a second synthetic nucleic acid molecule which encodes a reporter polypeptide which has at least 90% amino acid sequence identity to the reporter polypeptide encoded by the wild type nucleic acid sequence, wherein the codons in the second synthetic nucleic acid molecule that are different than the codons in the wild type nucleic acid sequence are mammalian high usage codons selected to result in the second synthetic nucleic acid molecule having at least 3-fold fewer a-reduced number of a combination of different mammalian transcription factor binding sequences, and optionally a reduced number of intron splice sites, poly(A) addition sites or prokaryotic 5' noncoding regulatory sequences relative to the wild type nucleic acid sequence, wherein the codons which differ in the first synthetic nucleic acid molecule relative to the second synthetic nucleic acid molecule are mammalian codons selected to result in the first synthetic nucleic acid molecule having a reduced number of a combination of different mammalian transcription factor binding sequences, and optionally a reduced number of intron splice sites, poly(A) addition sites or prokaryotic 5' noncoding regulatory sequences, that are introduced to the second synthetic nucleic acid molecule by selecting the mammalian high usage codons, wherein the mammalian transcription factor binding sequences are those present in a database of transcription factor binding sequences, wherein the wild type nucleic acid sequence and the synthetic sequence encode encodes chloramphenicol acetyltransferase, Renilla luciferase, beetle luciferase, beta-lactamase, beta-glucuronidase or beta galactosidase, and wherein the synthetic nucleic acid molecule has at least 95% nucleotide sequence identity to SEQ ID NO:9, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 297, SEO ID NO: 299, or SEQ ID NO: 301.

2-23. (Canceled).

24. (Currently Amended) The [[first]] synthetic nucleic acid molecule of claim 1 wherein the [[first]] synthetic nucleic acid molecule is expressed in a mammalian host cell at a level which is

greater than that of the wild type nucleic acid sequence.

25-34. (Canceled)

35. (Currently Amended) A plasmid comprising the [[first]] synthetic nucleic acid molecule

of claim 1.

36. (Currently Amended) An expression vector comprising the [[first]] synthetic nucleic acid

molecule of claim 1 linked to a promoter functional in a cell.

37. (Currently Amended) The expression vector of claim 36 wherein the [[first]] synthetic

nucleic acid molecule is operatively linked to a Kozak consensus sequence.

38. (Original) The expression vector of claim 36 wherein the promoter is functional in a

mammalian cell.

39. (Original) The expression vector of claim 36 wherein the promoter is functional in a

human cell.

(Canceled).

41. (Original) The expression vector of claim 36 wherein the expression vector further

comprises a multiple cloning site.

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- 42. (Currently Amended) The expression vector of claim 41 wherein the expression vector comprises a multiple cloning site positioned between the promoter and the [[first]] synthetic nucleic acid molecule.
- 43. (Currently Amended) The expression vector of claim 41 wherein the expression vector comprises a multiple cloning site positioned downstream from the [[first]] synthetic nucleic acid molecule.
- (Previously Presented) An isolated host cell comprising the expression vector of claim
  36.
- 45. (Currently Amended) A kit comprising, in suitable container means, the expression vector of claim 36, wherein the first synthetic nucleic acid molecule encodes a reporter molecule.
- 46. (Canceled).
- 47. (Previously Presented) A [[first]] polynucleotide which hybridizes under high stringency hybridization conditions to the synthetic nucleic acid molecule of claim 1 or the complement thereof SEQ ID NO:9 (GRver5.1), SEQ ID NO:18 (RD156-1H9), SEQ ID NO:297 (GRver5.1), SEQ ID NO:301 (RD156-1H9), or the complement thereof, and comprises an open reading frame encoding a beetle luciferase polypeptide which has at least 90% amino acid sequence identity to a luciferase having SEQ ID NO:23 encoded by a corresponding wild type nucleic acid sequence having SEQ ID NO:1, wherein the codon composition of the open reading frame of the first polynucleotide is different at more than 25% of the codons from that of the wild type luciferase nucleic acid sequence and is different than the codon composition of a second polynucleotide which encodes a polypeptide which has at least 90% amino acid sequence identity to the polypeptide encoded by the wild type nucleic acid sequence, wherein the codons in the second polynucleotide that are different than the codons in the wild type nucleic acid sequence are mammalian high usage codons selected to result in the second-polynucleotide having a reduced number of a combination of different mammalian transcription factor binding

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sequences, intron splice sites, poly(A) addition sites or prokaryotic 5' noncoding regulatory sequences relative to the wild type nucleic acid sequence, wherein the codons which differ in the first polynucleotide relative to the second polynucleotide are mammalian codons selected to result in the open reading frame in the first polynucleotide having a reduced number of a combination of different mammalian transcription factor binding sequences, and optionally a reduced number of intron splice sites, poly(A) addition sites or prokaryotic 5' noncoding regulatory sequences, that are introduced to the second polynucleotide by selecting the mammalian high usage codons, wherein the mammalian transcription factor binding sequences are those present in a database of transcription factor binding sequences, wherein the conditions include hybridization at 42°C in a solution consisting of 5X SSPE (43.8 g/L NaCl, 6.9 g/L NaH<sub>2</sub>PO<sub>4</sub> H<sub>2</sub>O and 1.85 g/L EDTA, pH adjusted to 7.4 with NaOH), 0.5% SDS, 5X Denhardt's reagent and 100 µg/mL denatured salmon sperm DNA followed by washing in a solution comprising 0.1X SSPE, 1.0% SDS at 42°C when a probe of about 500 nucleotides in length is employed.

48-80. (Canceled).

- (Currently Amended) The [[first]] synthetic nucleic acid molecule of claim 1,67 or 74
  wherein the transcription factor binding sequence is at least 5 bases in length.
- (Currently Amended) The [[first]] polynucleotide of claim 47 [[or 78]] wherein the transcription factor binding sequence is at least 5 bases in length.

83-85. (Canceled)

86. (Currently Amended) The [[first]] synthetic sequence of claim 1 wherein the selection of mammalian high usage codons and mammalian codons also reduces the number of restriction endonuclease sites. Filing Date: August 24, 2000 Title: SYNTHETIC NUCLEIC ACID MOLECULE COMPOSITIONS AND METHODS OF PREPARATION

87. (Currently Amended) The [[first]] polynucleotide of claim 47 [[or 78]] wherein the selection of mammalian high usage codons and mammalian codons also reduces the number of restriction endonuclease sites.

88-96. (Canceled).